



## Complete Summary

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### **GUIDELINE TITLE**

Secondary prevention of coronary artery disease clinical practice guidelines.

### **BIBLIOGRAPHIC SOURCE(S)**

Kaiser Permanente Care Management Institute. Secondary prevention of coronary artery disease clinical practice guideline. Oakland (CA): Kaiser Permanente Care Management Institute; 2006 Mar. 117 p. [51 references]

### **GUIDELINE STATUS**

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

SCOPE  
METHODOLOGY - including Rating Scheme and Cost Analysis  
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## SCOPE

### **DISEASE/CONDITION(S)**

Coronary artery disease (CAD)

### **GUIDELINE CATEGORY**

Management  
Prevention  
Treatment

### **CLINICAL SPECIALTY**

Cardiology  
Family Practice

Internal Medicine  
Preventive Medicine

## **INTENDED USERS**

Advanced Practice Nurses  
Nurses  
Pharmacists  
Physician Assistants  
Physicians

## **GUIDELINE OBJECTIVE(S)**

To assist primary care physicians and other health care professionals in the treatment of patients with coronary artery disease in order to prevent subsequent cardiovascular (CV) events

## **TARGET POPULATION**

Patients with coronary artery disease in the outpatient primary care setting, care management programs, home health, skilled nursing facilities, and custodial care facilities

Inpatient and emergency department settings are not addressed

## **INTERVENTIONS AND PRACTICES CONSIDERED**

1. Angiotensin-converting enzyme (ACE) inhibitor therapy
2. Angiotensin II receptor blocker (ARB) therapy
3. Antiplatelet therapy
  - Aspirin
  - Clopidogrel
  - Ticlopidine
4. Beta blockers, including carvedilol, metoprolol CR/XL, bisoprolol, metoprolol tartrate
5. Lipid management
  - Statins
  - Dietary fat modification

**Note:** Dietary supplement therapy with vitamins C, E, B6, B12, beta carotene, and folic acid is considered but not recommended.

## **MAJOR OUTCOMES CONSIDERED**

- Mortality due to cardiac causes
- All cause mortality
- Hospitalization, including non-fatal myocardial infarction (MI), nonfatal stroke, transient ischemic attack (TIA), unstable angina, and revascularization procedures
- Side effects of treatment

## METHODOLOGY

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Searches of Electronic Databases

### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

Guidelines are developed using an "evidence-based methodology" and involve a systematic literature search, critical appraisal of the research design and statistical results of relevant studies, and grading of the sufficiency (quantity, quality, consistency, and relevancy) of the evidence for drawing conclusions.

During the guideline development process, the Guideline Development Team reviews evidence published in peer-reviewed scientific journals, existing evidence-based guidelines, and consensus-based statements from external professional societies and government health organizations, and clinical expert opinion of Kaiser Permanente regional specialty groups.

For details of the literature search, including databases searched and search terms for each clinical question, see the original guideline document.

### **NUMBER OF SOURCE DOCUMENTS**

Not stated

### **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Weighting According to a Rating Scheme (Scheme Given)

### **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

Refer to Table 2 in the Appendix in the original guideline document for the system for grading the strength of a body of evidence.

### **METHODS USED TO ANALYZE THE EVIDENCE**

Review of Published Meta-Analyses  
Systematic Review with Evidence Tables

### **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Guidelines are developed using an "evidence-based methodology" and involve a systematic literature search, critical appraisal of the research design and statistical results of relevant studies, and grading of the sufficiency (quantity, quality, consistency, and relevancy) of the evidence for drawing conclusions.

### **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

To develop the coronary artery disease (CAD) guidelines, released in March 2006, a multidisciplinary, interregional Guideline Development Team first met in September 2005 to define the scope of the guideline. Clin-eGuide (Wolters Kluwer), an outside vendor, then performed systematic reviews of the medical literature on each of the clinical questions identified by the Guideline Development Team, assembled the evidence, and developed draft recommendations for review by the Guideline Development Team. All of the recommendations and supporting evidence were reviewed by the Guideline Development Team in depth during two conference calls in January and March, 2006.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendations are classified as either "evidence-based (A-D, I)" or "consensus." Refer to the table below for full definitions.

- Evidence-based: sufficient number of high-quality studies from which to draw a conclusion, and the recommended practice is consistent with the findings of the evidence. A recommendation can also be considered "evidence-based" if there is insufficient evidence and no practice is recommended.
- Consensus: insufficient evidence and a practice is recommended based on the consensus or expert opinion of the Guideline Development Team.

### Label and Language of Recommendations\*

Label	Evidence-Based Recommendations
<b>Evidence-based (A)</b>	<p><b>Language:</b> <sup>a</sup> The intervention is strongly recommended for eligible patients.</p> <p><b>Evidence:</b> The intervention improves important health outcomes, based on good evidence, and the Guideline Development Team (GDT) concludes that benefits substantially outweigh harms and costs.</p> <p><b>Evidence Grade:</b> Good.</p>
<b>Evidence-based (B)</b>	<p><b>Language:</b> <sup>a</sup> The intervention is recommended for eligible patients.</p> <p><b>Evidence:</b> The intervention improves important health outcomes, based on 1) good evidence that benefits outweigh harms and costs; or 2) fair evidence that benefits substantially outweigh harms and costs.</p> <p><b>Evidence Grade:</b> Good or Fair.</p>
<b>Evidence-based (C)</b>	<p><b>Language:</b> <sup>a</sup> No recommendation for or against routine provision of the intervention. (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent options.)</p> <p><b>Evidence:</b> Evidence is sufficient to determine the benefits, harms,</p>

Label	Evidence-Based Recommendations
	<p>and costs of an intervention, and there is at least fair evidence that the intervention improves important health outcomes. But the GDT concludes that the balance of the benefits, harms, and costs is too close to justify a general recommendation.</p> <p><b>Evidence Grade:</b> Good or Fair.</p>
<b>Evidence-based (D)</b>	<p><b>Language:</b> <sup>a</sup> Recommendation against routinely providing the intervention to eligible patients.</p> <p><b>Evidence:</b> The GDT found at least fair evidence that the intervention is ineffective, or that harms or costs outweigh benefits.</p> <p><b>Evidence Grade:</b> Good or Fair.</p>
<b>Evidence-based (I)</b>	<p><b>Language:</b> <sup>a</sup> The evidence is insufficient to recommend for or against routinely providing the intervention.= (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent options.)</p> <p><b>Evidence:</b> Evidence that the intervention is effective is lacking, of poor quality, or conflicting and the balance of benefits, harms, and costs cannot be determined.</p> <p><b>Evidence Grade:</b> Insufficient.</p>
<b>Consensus-based</b>	<p><b>Language:</b> <sup>a</sup> The language of the recommendation is at the discretion of the GDT, subject to approval by the National Guideline Directors.</p> <p><b>Evidence:</b> The level of evidence is assumed to be "Insufficient" unless otherwise stated. However, do not use the A, B, C, D, or I labels which are only intended to be used for evidence-based recommendations.</p> <p><b>Evidence Grade:</b> Insufficient, unless otherwise stated.</p>
<p>For the rare consensus-based recommendations which have "Good" or "Fair" evidence, the evidence must support a different recommendation, because if the evidence were good or fair, the recommendation would usually be evidence-based. In this kind of consensus-based recommendation, the evidence grade should point this out, e.g., "Evidence Grade: Good, supporting a different recommendation."</p>	

[a] All statements specify the population for which the recommendation is intended.

\* Recommendations should be labeled and given an evidence grade. The evidence grade should appear in the rationale. Evidence is graded with respect to the degree it supports the specific clinical recommendation. For example, there may be good evidence that Drugs 1 and 2 are effective for Condition A, but no evidence that Drug 1 is more effective than Drug 2. If the recommendation is to use either Drug 1 or 2, the evidence is good. If the recommendation is to use Drug 1 in preference to Drug 2, the evidence is insufficient.

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## **METHOD OF GUIDELINE VALIDATION**

Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

The National Guideline Directors' Guideline Quality Committee reviewed and approved the guidelines in March 2006.

## **RECOMMENDATIONS**

### **MAJOR RECOMMENDATIONS**

Recommendations are identified as either "evidence-based (A-D, I)" or "consensus-based." For definitions of the levels of recommendations see the end of the "Major Recommendations" field.

#### **Summary**

#### **Definition of Coronary Artery Disease (CAD)**

These guidelines describe secondary prevention measures for patients with a diagnosis of ischemic heart disease based upon a history of angina, myocardial infarction (MI), coronary artery bypass surgery graft (CABG), percutaneous coronary intervention (PCI), or evidence of coronary artery disease on angiography or non-invasive testing. For treatment decisions involving patients with acute coronary syndromes, cardiology consultation is recommended.

#### **Angiotensin-Converting Enzyme (ACE) Inhibitor Therapy**

For most patients with CAD,\* angiotensin-converting enzyme (ACE) inhibitor therapy is recommended for long term use,\*\* unless contraindicated.

\* In the PEACE Trial, patients with stable coronary artery disease and preserved left ventricular systolic function had no benefit on the composite endpoint of cardiovascular death, MI, and coronary revascularization with the addition of an ACE-inhibitor to standard medical therapy. ACE-inhibition is, therefore, not required in such patients.

\*\* For patients on concomitant aspirin, low-dose aspirin is recommended.

#### ***Evidence-based***

#### **Angiotensin II Receptor Blocker (ARB) Therapy**

- A. Angiotensin II receptor blocker (ARB) therapy is recommended for the following patients with CAD who are intolerant to ACE inhibitors:
- Patients with CAD and diabetes with hypertension and microalbuminuria (or albuminuria)

- Patients with CAD and left ventricular systolic dysfunction (LVSD)
- For patients who are intolerant to ACE inhibitors, with CAD and hypertension (without either LVSD or diabetes), ARB therapy is an option equal to other antihypertensive medications.
  - For all other patients with CAD who are intolerant to ACE inhibitors, there is insufficient evidence to recommend for or against ARB therapy.

A: **Consensus-based**

B, C: **Evidence-based**

### **ACE Inhibitor + Aspirin**

For all patients with CAD taking low-dose aspirin, ACE inhibitor therapy may be safely recommended for long term use.

**Evidence-based**

### **ACE Inhibitor Plus ARB Therapy**

- For CAD patients, the routine addition of ARB therapy to ACE inhibitor therapy is not recommended.
- If ARBs are added to ACE inhibitors it should be done for clinical reasons, such as uncontrolled hypertension or insufficient vasodilation.
- This recommendation applies whether or not a patient is treated with a beta blocker.

A, B, C: **Consensus-based**

### **Antiplatelet Therapy: Aspirin**

- For all patients with CAD, daily aspirin (75 to 325 mg) is recommended indefinitely, unless there is clear contraindication such as active bleeding, major coagulopathy, or true aspirin allergy.
- For CAD patients on concomitant ACE Inhibitors, low-dose aspirin is recommended.

(NOTE: The lowest dose commercially available acetylsalicylic acid (ASA) in the United States is 81 mg.)

A: **Evidence-based**

B: **Consensus-based**

### **Antiplatelet Therapy: Clopidogrel Use in Stable Patients**

- In stable CAD patients who tolerate aspirin well (and who are not post-procedure), clopidogrel is not recommended as either a substitute for or in addition to aspirin.
- In stable CAD patients with contraindications to aspirin, clopidogrel is recommended as the antiplatelet of choice.

A, B: **Consensus-based**

### **Antiplatelet Therapy: Post-Procedure**

- A. Following coronary artery bare metal stent placement clopidogrel plus aspirin is recommended to be given for at least four weeks.
- B. Following coronary artery drug-eluting stent placement, clopidogrel plus aspirin is recommended to be given for at least three months and up to one year post-procedure to reduce the risk of thrombotic events.
- C. If there is presence of a rash after clopidogrel use, patients may be switched to ticlopidine.

A: **Evidence-based**

B, C: **Consensus-based**

### **Beta Blocker Therapy**

Beta blocker therapy is recommended for CAD patients unless contraindicated; specifically:

- A. For post-MI patients non-intrinsic sympathomimetic activity (non-ISA) beta blocker therapy is recommended.
- B. For post-MI patients non-ISA beta blocker therapy is recommended to be initiated within hours after MI and continued long term.
- C. For CAD patients with unstable angina, long term non-ISA beta blocker therapy is recommended.
- D. For CAD patients with chronic stable angina, long term non-ISA beta blocker therapy is recommended for treatment of symptoms.
- E. For CAD patients with silent ischemia, non-ISA beta blocker therapy is recommended.
- F. For patients with CAD, beta blocker therapy is recommended peri-operatively for vascular surgery or noncardiac surgery with general anesthesia.
- G. For patients at risk for CAD,\* beta blocker therapy is recommended peri-operatively for vascular surgery.

\* At risk for CAD is defined as having at least two of the following cardiac risk factors: age  $\geq 65$  years, hypertension, current smoking, serum cholesterol  $\geq 240$  mg/dL (6.2 mmol/L), diabetes mellitus.

(NOTE: Drugs without ISA are atenolol, betaxolol, bisoprolol, carvedilol, labetalol, nadolol, metoprolol, propranolol, and timolol. Drugs with ISA are acebutolol, and pindolol.)

A, D, F, G: **Evidence-based**

B, C, E: **Consensus-based**

### **CAD Plus Mild to Moderate Reversible Airway Disease or Chronic Obstructive Pulmonary Disease (COPD): Beta Blocker Therapy**

- A. For CAD patients with concomitant mild to moderate reversible airway disease or chronic obstructive pulmonary disease (COPD) cardioselective beta blockers are recommended.



- B. Discuss the risks and benefits of treatment with the patient and instruct the patient to report any increase in airway symptoms.
- C. Initiating beta blocker therapy is NOT recommended:
  - For patients with severe airway disease requiring frequent hospitalization or intubation
  - During acute exacerbation of airway disease
  - When airway disease is unstable or poorly controlled

A: ***Evidence-based***

B, C: ***Consensus-based***

### **CAD Plus Heart Failure: Beta Blocker Therapy**

- A. For CAD patients with either left ventricular systolic dysfunction (LVSD) (New York Heart Associations (NYHA) Class II-IV) or asymptomatic LVSD (NYHA Class I), beta blockers are strongly recommended.
- B. For CAD patients with LVSD carvedilol, metoprolol CR/XL, or bisoprolol is the recommended choice of beta blocker therapy.
- C. Metoprolol tartrate (short-acting formulation) titrated to maximum tolerated dosage, is an acceptable but less well-established alternative to carvedilol, metoprolol CR/XL, or bisoprolol.

A, B: ***Evidence-based***

C: ***Consensus-based***

### **Lipid Management**

Treatment with statins is recommended for all adults with established atherosclerosis, even if baseline low density lipoprotein (LDL)-C is <100 mg/dL.

***Evidence-based***

### **Diet Therapy**

For all patients with CAD a diet rich in fruits, vegetables, legumes, nuts, whole grains, and n-3- (omega-3) polyunsaturated fat is recommended.

***Evidence-based***

### **Dietary Fat Modification**

For all patients with CAD consuming a usual Western diet the following modifications in dietary fat are recommended:

- Increase intake of n-3 (omega-3) polyunsaturated fatty acids to a level of approximately 1 g/day from a variety of sources (flaxseed, canola, and soybean oils, nuts, fish, and fish oil supplements).\*
- Replace saturated fatty acids with polyunsaturated and monounsaturated fatty acids.
- Reduce or eliminate intake of trans-fatty acids.

\* To limit the bioaccumulation of methylmercury, polychlorinated biphenyls (PCBs), dioxins, and other environmental contaminants, intake of certain fish (e.g., swordfish, tuna, and farmed salmon) is recommended not to exceed two servings per week.

### ***Consensus-based***

#### **Dietary Supplement Therapy**

- A. For patients with CAD, supplemental vitamins C, E and beta carotene are not recommended for prevention of cardiovascular mortality or subsequent coronary events.
- B. For CAD patients who are current or former smokers, supplemental beta carotene is not recommended due to a small but significant excess in all cause mortality reported in this group.
- C. For patients with CAD supplemental folic acid, vitamin B6, and vitamin B12 are not recommended.

A, B: ***Evidence-based***

C: ***Evidence-based (D)\****

\* Please note that only recommendations approved since the adoption in 2006 of evidence grading will use letters (A, B, C, etc.) to specify the grade of the evidence. Recommendations approved prior to 2006 will not include a letter grade following the statement "evidence-based."

#### **Definitions:**

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degree it supports the specific clinical recommendation. For example, there may be good evidence that Drugs 1 and 2 are effective for Condition A, but no evidence that Drug 1 is more effective than Drug 2. If the recommendation is to use either Drug 1 or 2, the evidence is good. If the recommendation is to use Drug 1 in preference to Drug 2, the evidence is insufficient.

### **CLINICAL ALGORITHM(S)**

An algorithm on Statin Management in Secondary Prevention is provided in the original guideline document.

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

### **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The type of supporting evidence is not specifically stated for each recommendation, but the evidence underlying the recommendations are drawn from randomized controlled trials, meta-analyses, and existing systematic reviews. In cases where the data was inconclusive, inconsistent, or non-existent, recommendations were based on the consensus opinion of the group.

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

Appropriate treatment and management of adult patients with coronary heart disease to decrease morbidity and mortality and improve patient outcomes

### **POTENTIAL HARMS**

Side effects of medication

## **CONTRAINDICATIONS**

### **CONTRAINDICATIONS**

Aspirin therapy is contraindicated in patients with active bleeding, major coagulopathy or aspirin allergy

## **QUALIFYING STATEMENTS**

### **QUALIFYING STATEMENTS**

- These guidelines are informational only. They are not intended or designed as a substitute for the reasonable exercise of independent clinical judgment by practitioners, considering each patient's needs on an individual basis.
- Guideline recommendations apply to populations of patients. Clinical judgment is necessary to design treatment plans for individual patients.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

### IMPLEMENTATION TOOLS

Pocket Guide/Reference Cards

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Kaiser Permanente Care Management Institute. Secondary prevention of coronary artery disease clinical practice guideline. Oakland (CA): Kaiser Permanente Care Management Institute; 2006 Mar. 117 p. [51 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2006 Mar

### GUIDELINE DEVELOPER(S)

Kaiser Permanente Care Management Institute - Managed Care Organization

### SOURCE(S) OF FUNDING

Kaiser Permanente Care Management Institute

### GUIDELINE COMMITTEE

Kaiser Permanente CAD Guidelines Project Management Team  
Kaiser Permanente CAD Guidelines Development Team

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

*Kaiser Permanente CAD Guidelines Project Management Team Members:* John Golden, MD, Clinical Lead, Care Management Institute; Donna M. Schaffer, RD, MPH, Project Manager, Care Management Institute; Paul Barrett, MD, Evidence-Based Medicine Methodologist, Care Management Institute; Tabitha Pousson, Staff Assistant, Care Management Institute

*Kaiser Permanente CAD Guidelines Development Team Members:* John H. Merenich, MD, Cardiology, KP Colorado; George Kawamura, MD, Cardiology, KP Georgia; Alan Golston, MD, Cardiology, Group Health Cooperative; Art Resnick, MD, Cardiology, Group Health Cooperative; Steven Hong, MD, Internal Medicine, KP Hawaii; Patricia E. Casey, MSN, RN, Chronic Disease Management, KP Mid-Atlantic States; John Golden, MD, Cardiology, KP Mid-Atlantic States; Gerald Bourne, MD, Cardiology, KP Northern California; Carlos Iribarren, MD, CVD Research, KP Northern California; Marc Jaffe, MD, Endocrinology, KP Northern California; Eleanor Levin, MD, Cardiology, KP Northern California; Anita Strohmeier, Chronic Disease Management, KP Northern California; Wiley V. Chan, MD, Internal Medicine, KP Northwest; Alison Fulmer, MD, Cardiology, KP Northwest; Shobana Rajagopal, MD, Family Practice, KP Northwest; Maan Fares, MD, Cardiology, KP Ohio; Carol Bartolotto, MPH, RD, Health Education, KP Southern California; Victor M. Benson, MD, Internal Medicine, KP Southern California; Gary M Besinque, PharmD, Pharmacy, KP Southern California; Kathleen Ryman, MD, Cardiology, KP Southern California

## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Not stated

## **GUIDELINE STATUS**

This is the current release of the guideline.

## **GUIDELINE AVAILABILITY**

Electronic copies: None available

Print copies: Available from the Kaiser Permanente Care Management Institute, One Kaiser Plaza, 16L, Oakland, CA 94612

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following is available:

- Kaiser Permanente Care Management Institute. Summary of secondary prevention of coronary artery disease clinical practice guidelines. Oakland (CA): Kaiser Permanente Care Management Institute; 2006 Mar. 10 p.

Electronic copies: None available

Print copies: Available from the Kaiser Permanente Care Management Institute, One Kaiser Plaza, 16L, Oakland, CA 94612

The following is also available:

- Pocket card: coronary artery disease in primary care. Oakland (CA): Kaiser Permanente Care Management Institute; 2006. 2 p.

Electronic copies: None available

Print copies: Contact the CMI Product Line at (510) 271-6426 or [CMIProducts@kp.org](mailto:CMIProducts@kp.org).

## **PATIENT RESOURCES**

None available

## **NGC STATUS**

This NGC summary was completed by ECRI on November 17, 2006. The information was verified by the guideline developer on December 19, 2006.

## **COPYRIGHT STATEMENT**

For any questions regarding the content of this Kaiser Permanente National Clinical Practice Guideline, please contact Donna M. Schaffer, RD, MPH, CMI at [Donna.M.Schaffer@kp.org](mailto:Donna.M.Schaffer@kp.org) or (510) 271-5678.

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